BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 58, NO. 6, SEPTEMBER 1982

CYSTOID MACULAR EDEMA OF NONRETINAL VASCULAR ORIGIN*

BARRY E. WRIGHT, M.D.

Assistant Professor of Ophthalmology
Department of Ophthalmology
Montefiore Hospital and Medical Center
Bronx, New York

CYSTOID macular edema results from accumulation of extracellular fluid within the outer plexiform layer in the macular region. Because of the anatomic configuration of this region, cystoid spaces are formed. A wide variety of disease entities of nonretinal vascular etiology are associated with cystoid macular edema. It is beyond the scope of this presentation to include all of these disease processes, and it will focus on the most commonly encountered examples of four different disease categories: inflammatory, hereditary, toxic, and degenerative.

INFLAMMATORY

Pars planitis is the term used to describe a common form of peripheral uveitis of unknown etiology. It may involve, in varying degrees of

*Presented before the Section on Ophthalmology of the New York Academy of Medicine October 20, 1980.

severity, the pars plana of the ciliary body, the angle of the anterior chamber, the pars ciliaris of the ciliary body, and the peripheral retina near the ora serrata, including the retinal vessels.[1] The resultant clinical appearance is that of significant amounts of cellular exudative debris which cover the pars plana and ora serrata to produce gelatinous "snowbanks" and associated exudative debris in the vitreous humor.[2] Occurring most commonly in those under the age of 50, it frequently develops gradually and presents with relatively mild symptoms. 70 to 80% become bilateral, but the ultimate visual prognosis is good and 80% recover visual function without any treatment. Therapeutic intervention is usually reserved for that 20% who develop cystoid macular edema. Fluorescein angiography is most useful in evaluating this process and in determining its severity by measurement of the amount of fluorescein leakage from the perifoveal capillaries (Figures 1*a*-1*c*). Although systemic and topical corticosteroids have been utilized in the past, periocular (i.e., subconjunctival or sub-Tenon's capsule) corticosteroids seem to be the treatment of choice. In refractory cases, systemic immunosuppresive agents may be necessary. Despite these efforts, 28% may develop permanent changes in the macula which impair vision.[3]

Hereditary

Retinitis pigmentosa is an inherited tapetoretinal degeneration which diffusely involves the photoreceptors and retinal pigment epithelium. It remains obscure as to which of these two layers of the retina is involved initially by this progressive abiotrophy, or if indeed they deteriorate simultaneously. In addition to typical visual field deficits and electrophysiological changes (extinguished electroretinogram), these patients may eventually lose central vision. While much of this loss may be due to the disease of the macular photoreceptors and retinal pigment epithelium, it is becoming increasingly clear that cystoid macular edema also plays a role in the further loss of central visual function. Fishman's group at the University of Illinois Eye and Ear Infirmary reported that 15% of 110 consecutive patients with retinitis pigmentosa had cystoid macular edema.[4,5] Fetkenhour reported that 70% of 58 consecutive retinitis pigmentosa patients at Northwestern University had cystoid macular edema when examined by fluorescein angiography.[6] The large discrepancy in the cases reported by these two major referral centers may in part be due to difficulty in making the proper diagnosis in these patients. Fluorescein

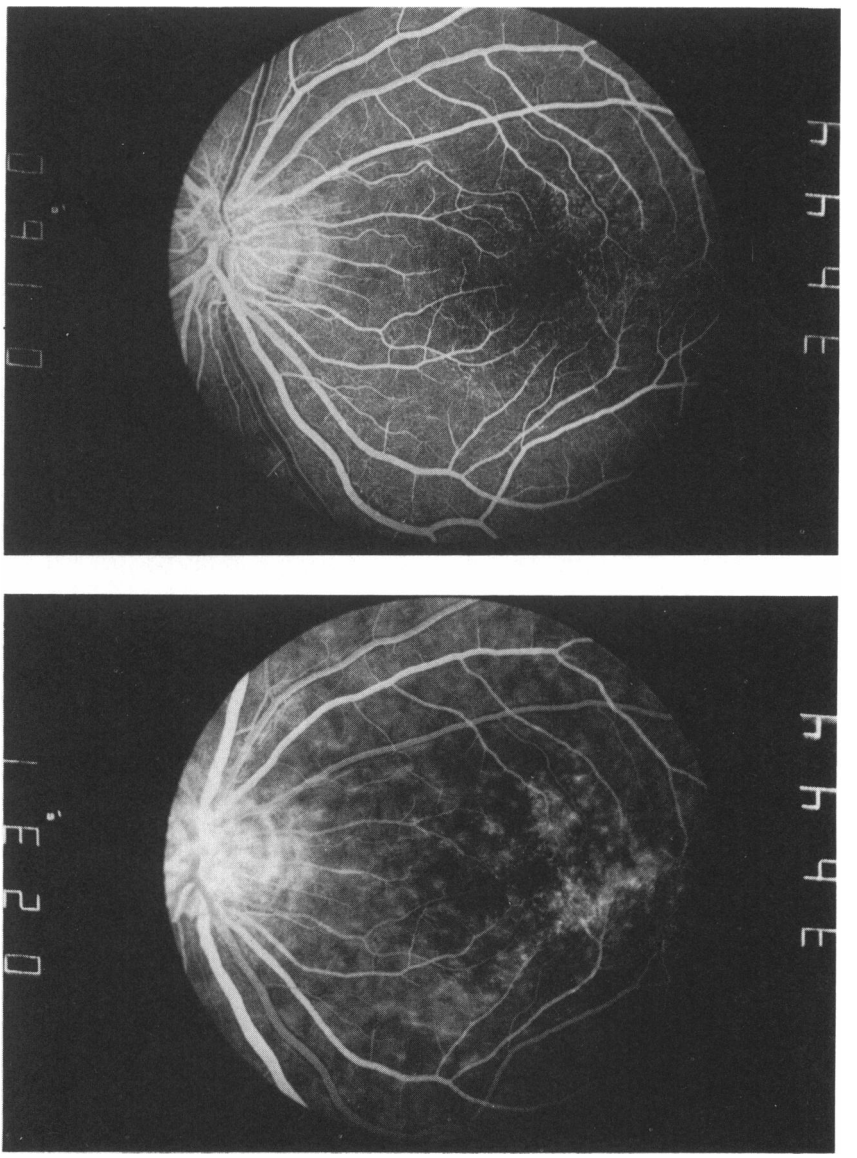

Fig. 1*a*,1*b*. Fluorescein angiogram of the macula in a patient with pars planitis demonstrating progressive leakage of fluorescein from the perifoveal capillaries.

angiography is essential in such patients because the characteristic leakage pattern may appear only in the very late phases (Figures 2*a*-2*c*). This is especially true among those who have become photophobic, which makes

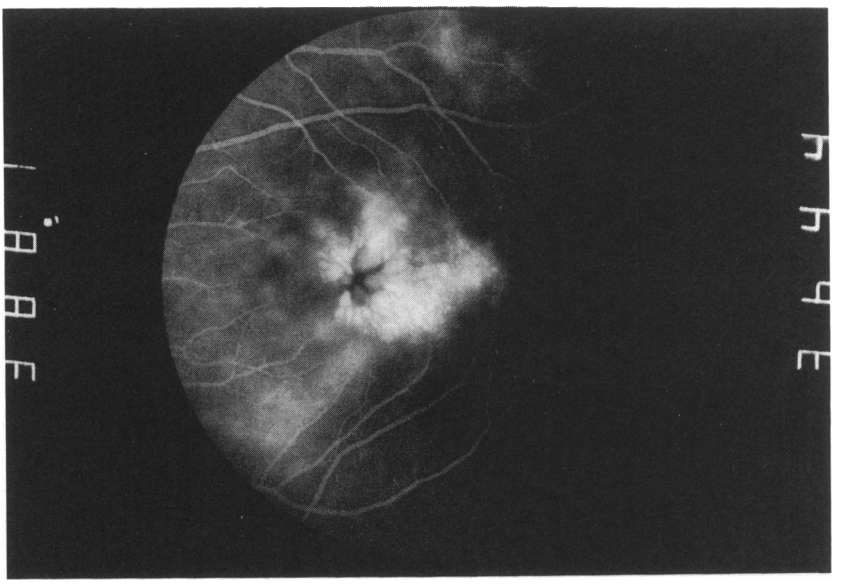

Fig. 1*c*. Late phase demonstrates accumulation of dye into cystoid spaces, forming a petaloid pattern in the macula.

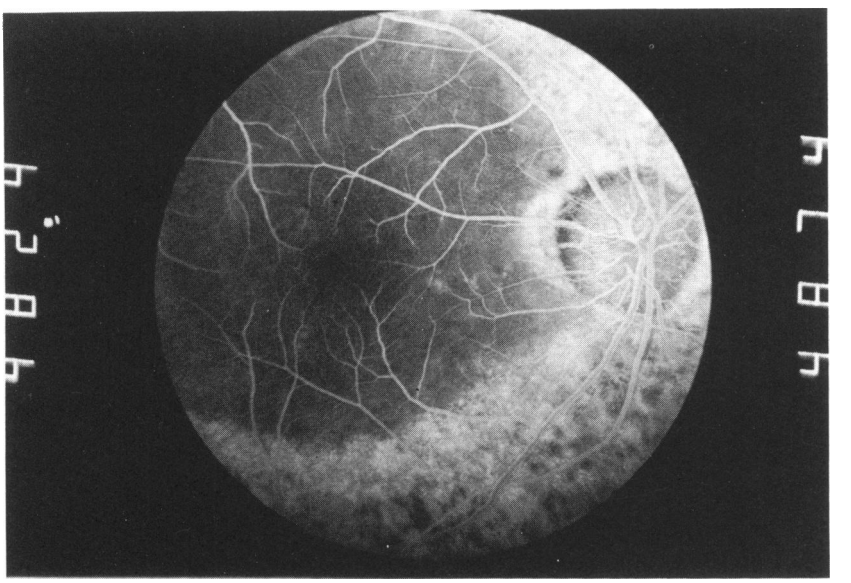

Fig. 2*a*. Early phase of a fluorescein angiogram of the macula in a patient with retinitis pigmentosa showing no leakage of dye.

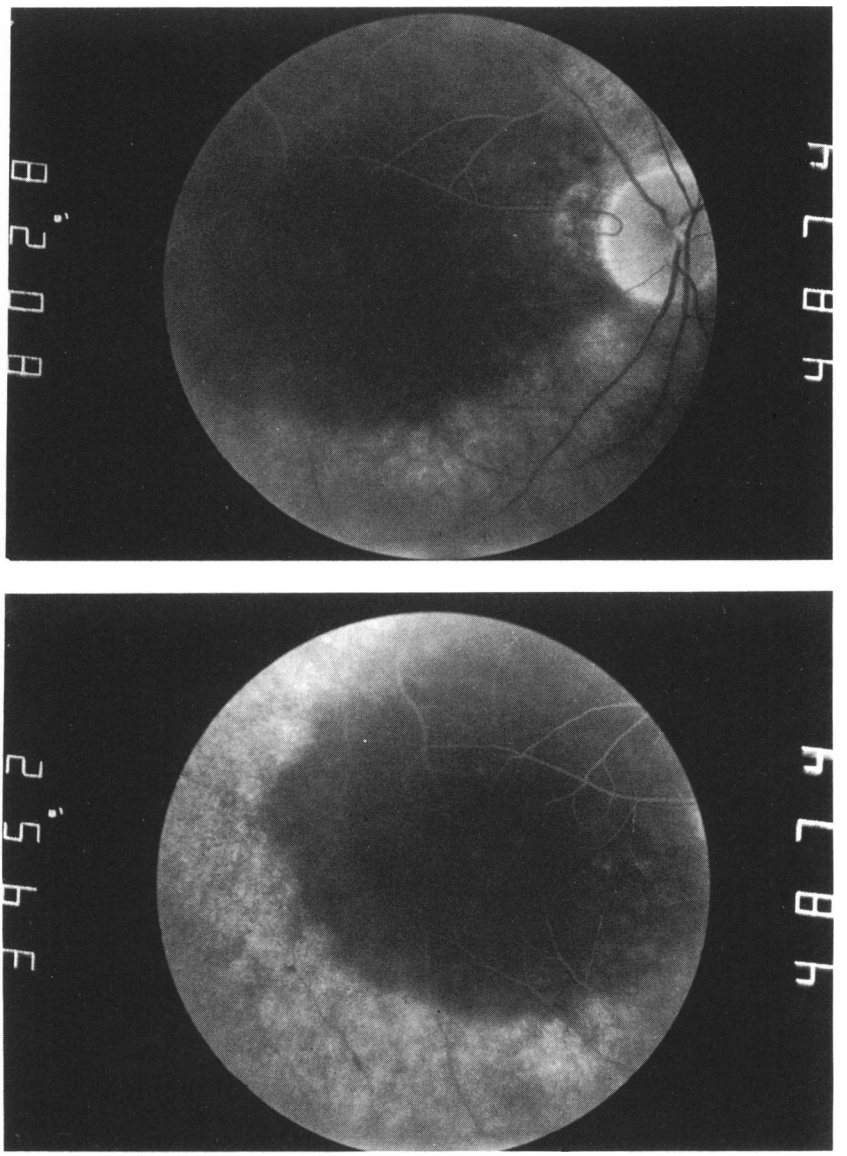

Fig. 2*b*,2*c*. Only in the very latest phases is there sufficient leakage of fluorescein to form cystoid macular edema.

clinical biomicroscopic evaluation of the macula difficult when the amount of macular edema may be slight. Unfortunately, there is no effective treatment for the cystoid macular edema in such cases or for the underlying disease process.

Toxic

In 1968 Kolker and Becker[7] described a series of aphakic patients who received topical epinephrine as treatment for their glaucoma and subsequently lost vision because of development of cystoid macular edema (Figure 3*a*). Unable to determine the cause of the cystoid macular edema, all medications were discontinued and the cystoid edema eventually resolved (Figure 3*b*). To determine whether this was indeed related to the instillation of the topical epinephrine, they reinstituted therapy with topical epinephrine alone. They found that in this susceptible group cystoid macular edema not only recurred (Figure 3*c*), but once again resolved following discontinuance of the medication (Figure 3*d*). Subsequent studies by Michels and Maumenee[8] at the Wilmer Institute and by MacKool's group[9] at the New York Eye and Ear Infirmary further substantiated the susceptibility of aphakic eyes to topical epinephrine because 20 to 30% developed cystoid macular edema. While topical epinephrine may indeed be necessary adequately to treat an aphakic patient with glaucoma, this toxic side effect must be kept in mind should the patient develop visual loss. The treatment of choice at that point would be to discontinue the offending medication.

Degenerative

Idiopathic preretinal macular gliosis was definitively described as a distinct clinical entity by the late George N. Wise[10] in 1975 with complete clinicopathologic correlation.[11] A fine glial membrane penetrates the internal limiting membrane of the retina and grows along the surface of the retina, to result in a subtle glistening or cellophane appearance. It may produce traction on the superficial retinal tissues and throw them into fine folds (Figure 4). As it becomes more prolific, it may produce traction on the retinal vasculature, causing subsequent tortuosity or straightening of the vessels (Figure 5*a*, 5*b*). With increasing traction, breakdown of the blood-retinal barrier may occur and result in the accumulation of increasing amounts of fluid in the affected area and the formation of cystoid macular edema (Figures 5*c*, 5*d*).

This is a relatively common retinal disorder among those over the age of 50. While there are no exact figures as to the incidence, it is estimated that it has a prevalence of 2% in the population more than 50 years of age and that a third of these have the disorder bilaterally.[12] It is uncommon in the young, and 95% of all cases occur in patients over the age of 50. Most

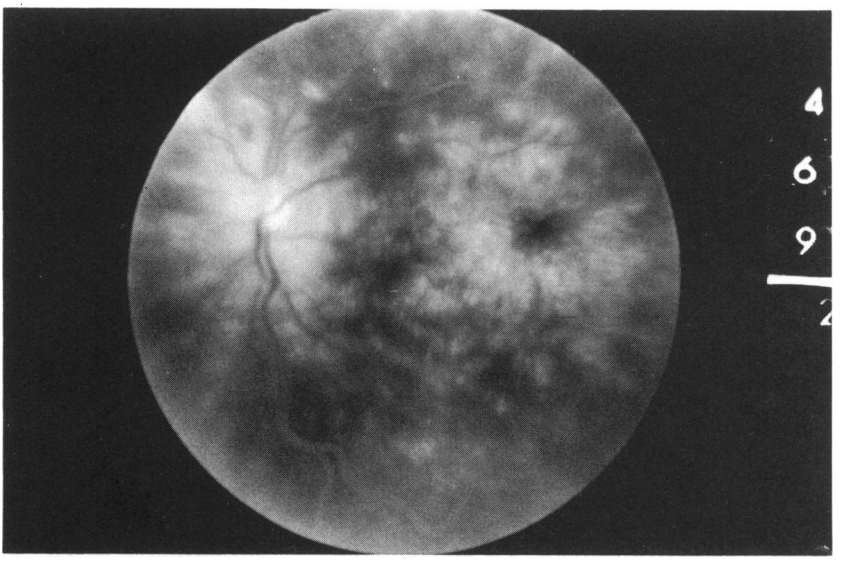

Fig. 3*a*. Late phase of a fluorescein angiogram in an aphakic patient who developed cystoid macular edema after receiving topical epinephrine.

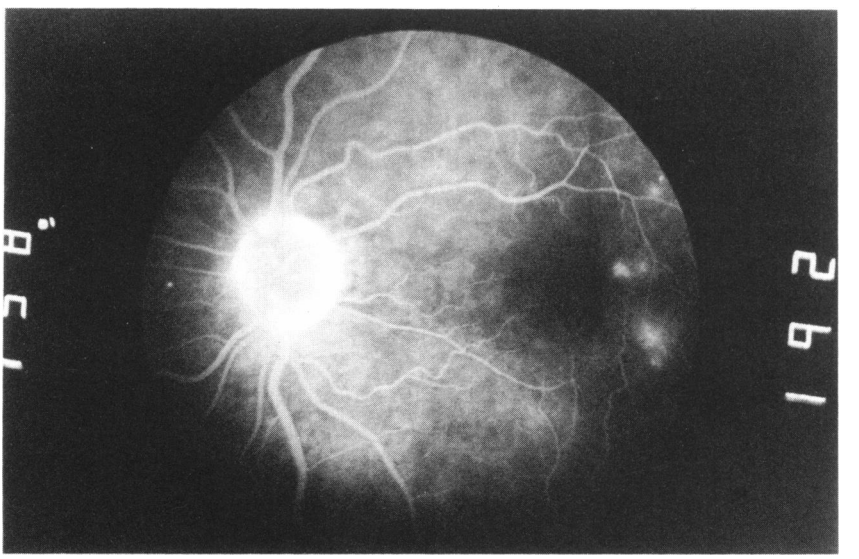

Fig. 3*b*. Fluorescein angiogram of the same patient (3*a*) taken several months after topical epinephrine was discontinued showing resolution of cystoid macular edema.

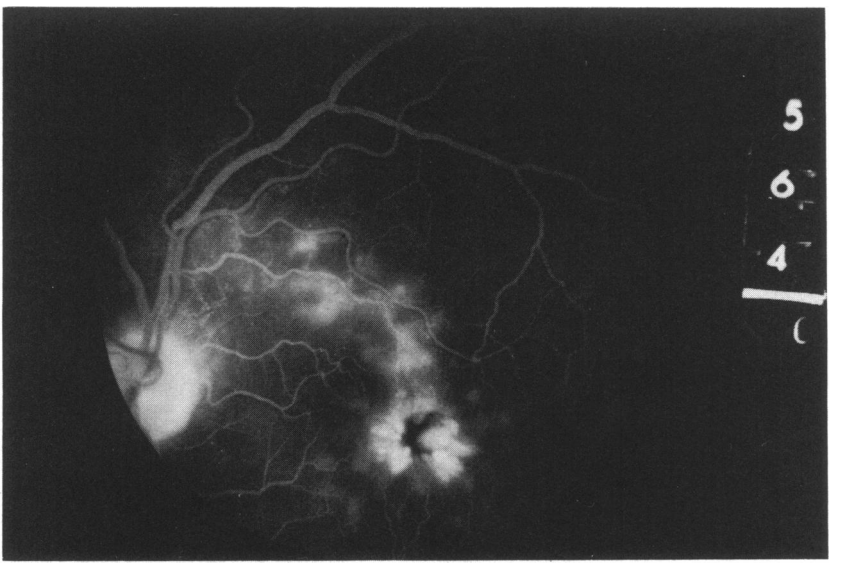

Fig. 3*c*. Fluorescein angiogram of a similar aphakic patient in whom it was necessary to reinstitute topical epinephrine. Cystoid macular edema recurred.

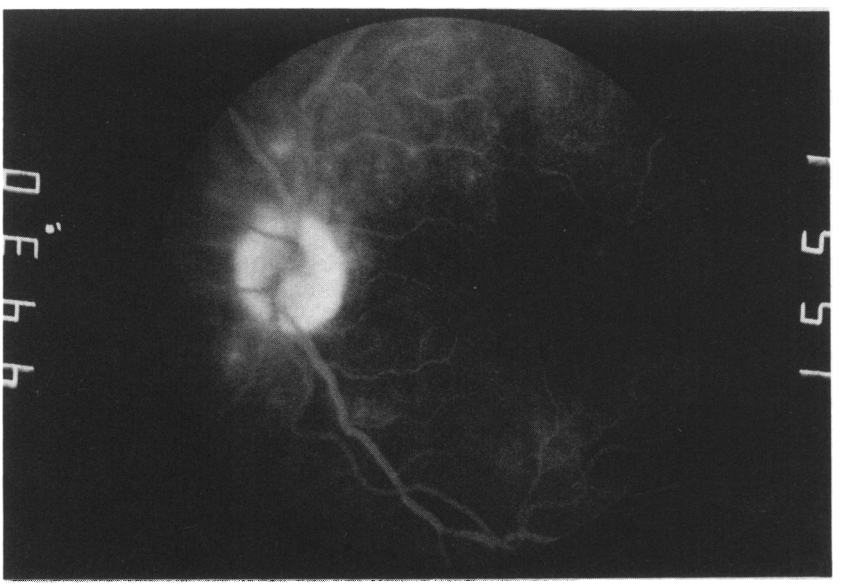

Fig. 3*d*. Same patient (3*c*) three months after discontinuance of topical epinephrine showing resolution of cystoid macular edema.

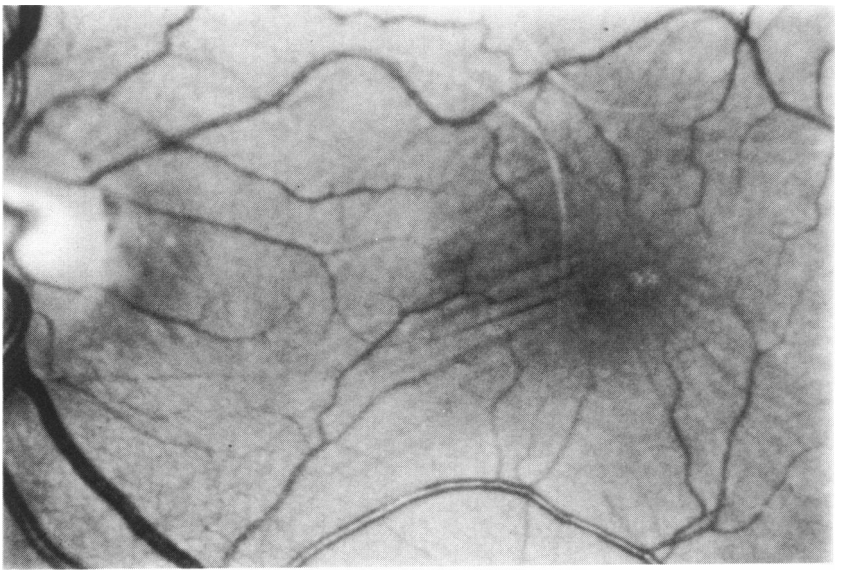

Fig. 4. Preretinal gliotic membrane which has produced fine retinal striae secondary to traction.

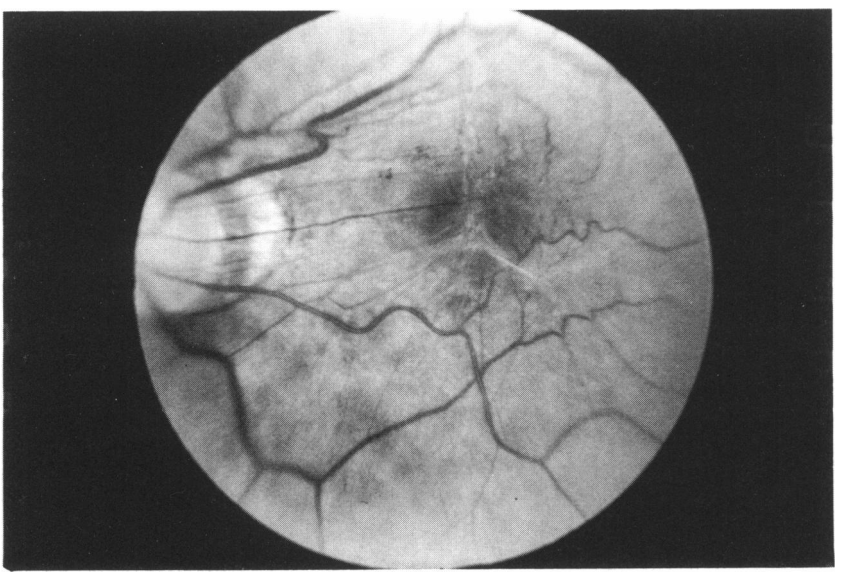

Fig. 5*a*. A severe preretinal gliotic membrane which overlies the macula.

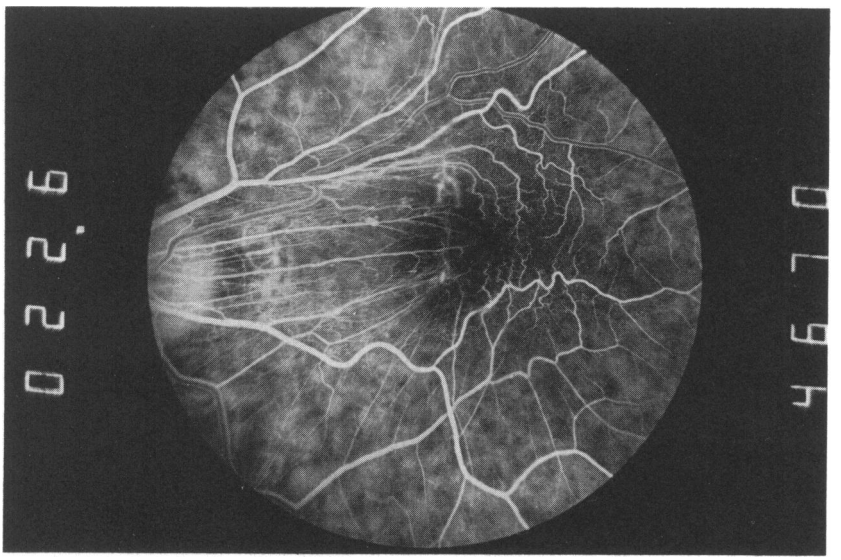

Fig. 5*b*. Fluorescein angiogram demonstrating straightening of retinal vessels due to traction by the gliotic membrane.

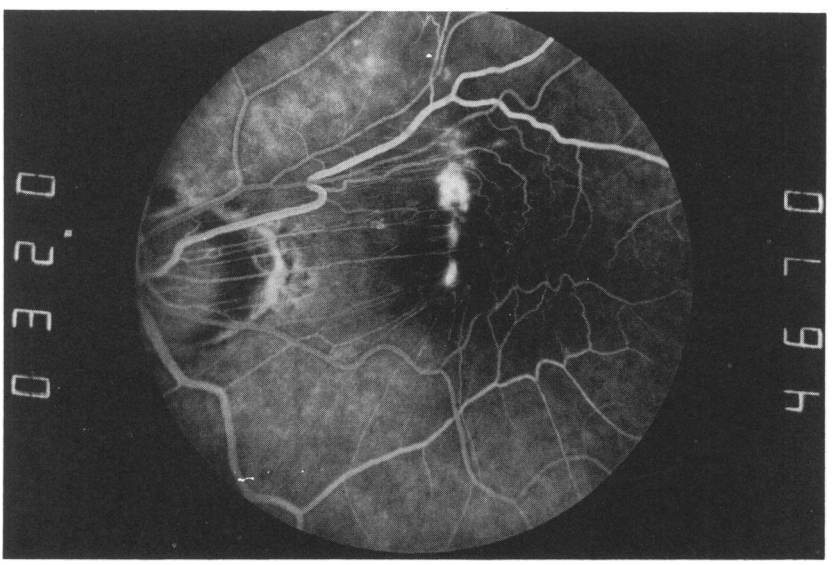

Fig. 5*c*. Later phase of the angiogram demonstrating progressive leakage of fluorescein through the vessel walls due to the traction.

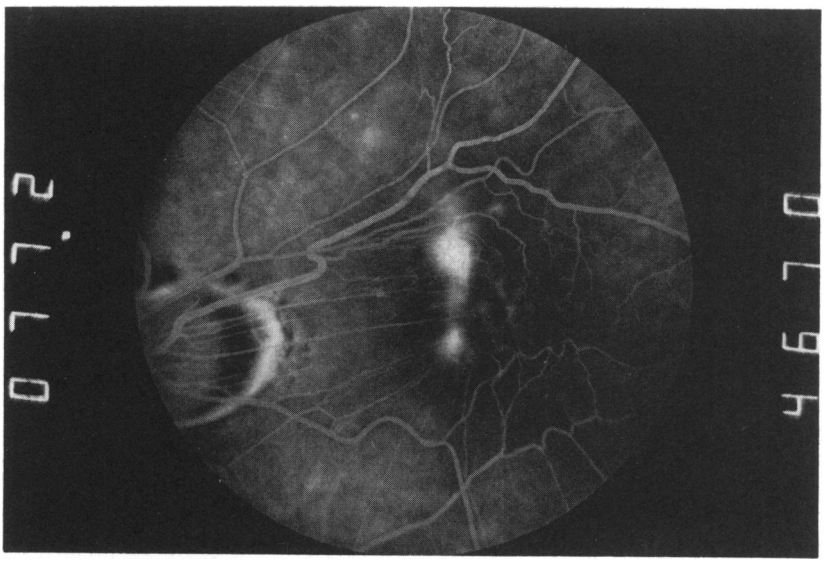

Fig. 5*d*. Late phase demonstrating accumulation of dye into cystoid macular edema.

patients are asymptomatic and have normal or near normal vision. In a large retrospective study which continued the work of Dr. Wise at Montefiore Hospital and Medical Center, 66% of the patients had vision of 20/30 or better.[12] In fact, there was no evidence of significant progression in more than 80% of these patients who had been followed for up to 20 years. Only in advanced disease, where marked proliferation of the gliotic membrane produces significant traction and breakdown of the blood-retinal barrier, is cystoid macular edema seen. This occurs in 15% of reported cases and may progress to the development of macular cysts or lamellar macular holes. Despite this, fewer than 5% develop vision worse than 20/200. Unfortunately, little can be done to treat any stage of this disease. The presence of the preretinal gliotic membrane makes photocoagulation untenable because the heat generated frequently stimulates additional proliferation or contraction of the membrane or both. Vitreous surgery to relieve traction may be considered in severe cases.

SUMMARY

The presence of the blood-retinal barrier (analogous to the blood-brain barrier) normally prevents the accumulation of extracellular fluid in the retina. Whenever this is disrupted, whether at the level of the retinal

vascular endothelium or of the retinal pigment epithelium, fluid may accumulate in the outer plexiform layer of the retina and form cystoid spaces. This cystoid macular edema is most commonly seen following intraocular surgery or secondary to retinal vascular disease. It is important to remember, however, that disease entities of nonretinal vascular origin may also produce cystoid macular edema. We have, therefore, presented examples of inflammatory, hereditary, toxic, and degenerative disease processes which are associated with cystoid macular edema.

REFERENCES

1. Gartner, J.: The fine structure of the vitreous base of the human eye and the pathogenesis of pars planitis. *Am. J. Ophthalmol. 71*:1317-27, 1971.
2. Maumenee, A.E.: Clinical entities in uveitis: An approach to the study of intraocular inflammation. *Am. J. Ophthalmol. 69*: 1-27, 1970.
3. Smith, R.E., Godfrey, W.A., and Kimura, S.J.: Chronic cyclitis: I. Course and visual prognosis. *Trans. Am. Acad. Ophthalmol. Otolaryngol. 77*:760-68, 1973.
4. Fishman, G.A., Fishman, M., and Maggiano, J.: Macular lesions associated with retinitis pigmentosa. *Arch. Ophthalmol. 95*:798-803, 1977.
5. Fishman, G.A., Maggiano, J.M., and Fishman, M.: Foveal lesions seen in retinitis pigmentosa. *Arch. Ophthalmol. 95*:1993-96, 1977.
6. Fetkenhour, C.L., Choromokos, E., Weinstein, J., and Shoch, D.: Cystoid macular edema in retinitis pigmentosa. *Trans. Am. Acad. Ophthalmol. Otolaryngol. 83*:515-21, 1977.
7. Kolker, A.E. and Becker, R.: Epinephrine maculopathy. *Arch. Ophthalmol. 79*:552-62, 1968.
8. Michels, R.G. and Maumenee, A.E.: Cystoid macular edema associated with topically applied epinephrine in aphakic eyes. *Am. J. Ophthalmol. 80*:379-88, 1975.
9. MacKool, R.J., Muldoon, T., Fortier, A., and Nelson, D.: Epinephrine-induced cystoid macular edema in aphakic eyes. *Arch. Ophthalmol. 95*:791-93, 1977.
10. Wise, G.N.: Clinical features of idiopathic preretinal macular fibrosis. *Am. J. Ophthalmol. 79*:349-57, 1975.
11. Bellhorn, M.S., Friedman, A.H., Wise, G.N., and Henkind, P.: Ultrastructure and clinicopathologic correlation of idiopathic preretinal macular fibrosis. *Am. J. Ophthalmol. 79*:366-73, 1975.
12. Yagoda, A.D., Walsh, J.B., and Henkind, P: Idiopathic Preretinal Macular Gliosis. In: *International Ophthalmology Clinics*, Rabb, M., editor. Boston, Little, Brown, 1981, pp. 107-18.